SÉZARY SYNDROME PART TWO: TREATMENT OPTIONS

In the treatment of Sézary syndrome, we have yet to establish a unified algorithm to map out which drugs to use and when to use them. This lack of uniformity is due in large part to the equivocal efficacy of most treatments, usually in the 35% response rate range, meaning that no specific treatment is clearly superior. Furthermore, treatment strategy is very nuanced and individualized based on many patient factors including patient comorbidities, prior treatment failures and access to specific treatments.

Research is underway exploring genomics in CTCL which aims to allow clinicians to match drug choice to patients’ disease molecular profiles.

Physicians are increasingly utilizing combination therapies in treating Sézary syndrome. What drugs or therapies are selected is driven by the overall burden of malignant lymphocytes in the blood, lymph nodes and skin. As we select various treatments and combine them, it is with the goal of reducing disease in various body compartments in a customized fashion.

For those people with relatively few cancerous cells circulating in their bloodstream, treatment is usually a pairing of a systemic category A medication with a skin-directed therapy such as phototherapy or topical creams.

However, for individuals with many malignant cells circulating in their blood, systemic agents with good evidence of targeting the bloodstream are initiated. This group commonly includes targeted agents such as mogamulizumab, brentuximab, and alemtuzumab, HDAC inhibitors such as romidepsin as well as immunotherapies such as pembrolizumab and more classical chemotherapy agents like doxorubicin.

**Category A Medications**

In a review of category A medications, **Bexarotene** is a retinoid (Vitamin A analog), which helps to impose a more normal cellular differentiation cycle on abnormal lymphocytes which are proliferating unchecked in Sézary. It is available in capsules, and can be given alone or with other medications. The main side effects reported with bexarotene are suppressed thyroid function and an increase in blood cholesterol. Due to these predictable drug side effects, patients also are started on thyroid replacement and cholesterol lowering medications when starting bexarotene.

*Sézary Syndrome...continued on page 10*
What Is Cutaneous Lymphoma?
Cutaneous lymphomas are cancers of lymphocytes (white blood cells) that primarily involve the skin. Classification is based on lymphocyte type: B-lymphocytes (B-cell) or T-lymphocytes (T-cell). Cutaneous T-cell lymphoma (CTCL) is the most common type of cutaneous lymphoma that typically presents with red, scaly patches or thickened plaques of skin that often mimic eczema or chronic dermatitis. Progression from limited skin involvement is variable and may be accompanied by tumor formation, ulceration and exfoliation, complicated by itching and infections. Advanced stages are defined by involvement of lymph nodes, peripheral blood, and internal organs.

Cutaneous Lymphoma Foundation

A non-profit organization. Donations are tax deductible to the extent allowed by law.

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Lauren Carlson
Happy Holidays!

Here we are at the end of our second year impacted by the COVID-19 virus. The year 2021 has seen more coronavirus variants, multiple vaccination opportunities, continued mask-wearing, and even more questions about what we, as patients, should do to try and keep ourselves safe and healthy. The challenges continue and our organization is working tirelessly to meet the changing needs of our patient community.

The end of 2021 also marks my 10th anniversary as a member of the Board of Directors. When I recall my first board meeting in the fall of 2011, I remember feeling honored to be part of such a distinguished group of people, but I also remember feeling very intimidated and unsure about how I would be able to contribute to help make a difference in the lives of people affected by my disease. I had no medical background and, to be honest, the doctors who I had seen for the previous thirty years were competent, but none were very familiar with my disease and I always felt they were learning about it along with me. It was a shock to find myself surrounded by people who were not only more familiar with my disease than I was, but who were also very dedicated to specifically helping those of us who were affected by it. I will admit that I was almost afraid to speak at our meeting.

I have engaged in some way has made a difference.

Susan Thornton

“Each of you who has engaged in some way has made a difference.”

Susan Thornton

FROM THE CEO...continued on page 9

“"As a member of our community, you are never alone.”

Laurel Carlson

ISSUE 3, 2021
Dr. Michi Shinohara focused on how a new patient should be “worked up” or diagnosed. Most patients typically have a nodule on the skin that is biopsied. If the pathology report comes back with a diagnosis of B-cell lymphoma, it is important that imaging tests such as a CT scan or PET/CT scan are performed. While most B-cell lymphomas start in the lymph cells, these types of lymphomas start in the skin, so it is important to include imaging tests to look for an increase in the size of lymph nodes. Additional tests may also include flow cytometry (either of a skin biopsy or the peripheral blood) to test for abnormal B-cells in the blood. Dr. Shinohara also concluded that in most cases bone marrow biopsies were not necessary.

Dr. Zic mentioned that one of his takeaways from Dr. Shinohara’s presentation is that both pcMZL and pcFCL are typically slow growing and respond very well to treatment, except when pcFCL is found on the leg. For some reason, when the follicle center lymphomas are on the leg, they behave more aggressively and need to be watched more closely and may need more aggressive treatment than if they occur elsewhere on the body.

Dr. Guitart also spoke about other rare CBCL lymphomas, demonstrating, as noted by Dr. Zic, the complexity of high-grade B-cell lymphomas. Because of this complexity, Dr. Zic emphasized how important it is for individuals diagnosed with a high-grade B-cell lymphoma to have their biopsy slides read by a pathologist with B-cell lymphoma experience.

The outcomes of the group’s collaborative efforts have been published in the medical journal Blood. The publication of their report is significant to both physicians and pharmacological companies. For physicians, it can provide guidelines both in treating their patients and running trials at their facilities. For pharmacological companies, it can be used for designing trials, assessing patient response, and determining the endpoint of the trial in order to determine if it is successful. The outcomes of the group’s collaborative efforts could potentially help individuals diagnosed with cutaneous lymphoma, whether it be B or T-cell.

Low-Grade B-cell Lymphomas - Primary Cutaneous Marginal Zone Lymphoma and Follicle Center Lymphoma

Dr. Michi Shinohara presented on low-grade, or slow growing, cutaneous B-cell lymphomas. The two subtypes considered low-grade are the cutaneous follicle center lymphoma (pcFCL) and the cutaneous marginal zone B-cell lymphoma (pcMZL). Both have an excellent prognosis for patients.

Primary Cutaneous Lymphoma: International Collaborative Recommendations for Clinical Trial Design, Assessment, Response Criteria, Endpoints, and Update to Staging

About seven years ago, Dr. Elise Olsen brought together a group of cutaneous lymphoma experts from around the world to standardize how medications being studied in clinical trials for patients with cutaneous lymphoma. The group has worked towards developing criteria to determine the effectiveness of the medications being tested in clinical trials. Dr. Olsen presented the results of their collaboration which are soon to be published in the medical journal Blood.

The next speaker was Dr. Alejandro Guitart, MD, University of Virginia School of Medicine. The next speaker was Dr. Alejandro Guitart, MD, University of Virginia School of Medicine. The next speaker was Dr. Alejandro Guitart, MD, University of Virginia School of Medicine.

HELP ENSURE THE FUTURE OF THE CUTANEOUS LYMPHOMA FOUNDATION

Did you know you can support the Cutaneous Lymphoma Foundation in achieving its vision of a life free of cutaneous lymphoma and lower your tax bill with an IRA charitable rollover? If you have an IRA, or certain other types of retirement plans, and are at least 70 1/2 years old, you can reduce your income taxes (even if you don’t itemize) with a qualified charitable distribution (QCD) to the CL Foundation from your IRA. The donation can count as part of your required minimum distribution for 2021, thereby reducing your taxable income. So a charitable-minded account owner who must take out, say, $25,000, can divert part or all of it to his or her favorite charity, such as the CL Foundation. While the gift can’t be claimed as a charitable deduction, the payout doesn’t count as taxable income either. So a QCD doesn’t raise adjusted gross income in a way that could trigger higher income taxes, Medicare premiums, or taxes on Social Security benefits. Both Medicare Part B and Part D payments rise with income, so minimizing adjusted gross income can be important. A QCD is simple to make, however, there are some technical rules in that it cannot exceed $100,000, must be made directly to the Cutaneous Lymphoma Foundation by your IRA custodian, and must be completed by December 31.

Please check our website at https://bit.ly/3IHoAqQ for additional information about ways everyone can support the CL Foundation. If you have any questions or would like to discuss this further, please contact Holly Priece, COFO, at 248-644-9014 Ext. 200 and your personal estate planning attorney. 

The above summary is provided for informational purposes only and is not intended to be legal, tax or investment advice. Please contact your attorney or financial advisor for advice related to your personal circumstances.
LIVING WITH LYMPHOMATOID PAPULOSIS: A STORY OF HOPE

Shared by Victoria (Torie) M.

Most people think that the year 2020 was the year of COVID-19, but for us 2020 was the year that changed our lives forever. My name is Torie, my daughter’s name is Mia, and this is our story of hope.

Not Looking For a Diagnosis

In April 2019, Mia had a growth on her leg that just wouldn’t heal. It was going on six weeks and the lesion was getting necrotic. I have been working in dermatology for 20 years, so after two weeks of the growth not going away and getting better, I started applying cortisone. I even injected it with cortisone. The growth kept getting bigger and bigger. I asked a doctor who I had worked with to biopsy the growth to get rid of it, not looking for a diagnosis. We just thought it was an unusual bite from a weird arthropod. The diagnosis came back as “arthropod assault,” so it confirmed our thoughts because, until that day, we had not had a child with a form of CTCL come into our office. Fast forward to the end of November when a couple of lesions presented again. We kept thinking it was another arthropod assault and that Mia’s immune system was hypersensitive to bites now because of her skin’s experience with the bug bite from April.

Weeks went by again with no improvement, after trying topical and injectable cortisone and injectable cortisone therapies again which made the lesions worse. We started lightbox treatments, oral antibiotics and antiviral medications which weren’t making things better. We kept trying every topical treatment from rose hip oil, Manuka honey, even CBD cream. We live in Florida which has sunlight year round, but natural sunlight was not making it go away. Knowing what we know now, COVID-19 brought many stressors and stress doesn’t help matters. In the end, we decided to put Mia on methotrexate because other therapies were not working. She has been taking MTX for six months now.

On a Mission

I was on a mission to solve the mystery. I had been told by some doctors that “I should stop looking for the reason why this is happening because doctors can’t find the reason.” That was not acceptable to me. I said to myself, “How dare someone say those words to me, because I am A MOTHER WHO WILL FIND AN ANSWER FOR MY MIA.”

I subscribed to the Cutaneous Lymphoma Foundation newsletter, I reached out to patients in support groups, and searched daily to find the doctors that were well-versed with LyP. Dermatologists know about it, but not many know enough about the treatment options that are not typical. I found two doctors in Texas who know about LyP well. We were on the next plane to Houston, even in the middle of a pandemic. Many blood tests were done to try to figure out why this was happening. I had asked about a particular virus that I had read if exposed to it, it can cause this diagnosis. The blood test wasn’t run because the oncologist said he was running so many other levels to start. When I received the call about the blood test results, the oncologist stated that he was confused with Mia’s results because her T-cell levels showed a significant viral infection that potentially could have landed her in the hospital. I thought to myself, if he is confused then I am really confused as to how to proceed. Mia’s growths did not stop coming, so our quest for answers did not stop either.

Finding an Angel

I found the Cutaneous Lymphoma Foundation website when we were waiting for the final biopsy reports in January. I had watched every video three times and read every bit of information that was available on the site. I was looking for someone or something to answer my questions. I kept looking for any outlet that would give me the chance to connect with other parents who had children with lymphomatoid papulosis. Again, my career is in dermatology, but I didn’t have anyone to share this with or anyone who could help me with this process. I had found a couple of support groups for LyP patients but it was mostly patients in the groups.

I had FINALLY found an angel on the LyP Facebook group. The angel is named Mindy. Her daughter was 14 and looked just like Mia. Mindy was literally an angel sent to us. I finally had another parent to talk to. Our daughters were so similar and were both experiencing the same struggles. It was the first time I had someone who understood what we were going through. Her daughter was diagnosed with LyP a couple of years before Mia, so she really helped to guide me. There were only two other parents I connected with during these months because they were all I could find with children that have LyP. I would call the Foundation and countlessly look for any parent groups I could find to meet parents going through the same thing.

Never Stop Trying

I subscribed to the website, and I have really learned to appreciate the good days and most of all to never give up on hope.

Disclaimer - Stories of Hope are an amazing opportunity to share, grow and learn from a peer’s experiences. Stories of Hope are not intended to serve as medical advice; given the individual nature of a diagnosis, all diagnosis and treatment decisions should be made alongside your medical team.
I have developed a cutaneous patch around the vaccination site. Is this something I should be concerned about, particularly if I am getting a booster?

Some patients are reporting a rash around the vaccination site and you may get another rash with the booster, but it is still recommended to get the booster if you qualify for it.

Do you recommend that patients who were vaccinated prior to being six months off rituximab vaccinate again after being nine months off rituximab?

Most people who have received rituximab did not mount an immune response from the COVID-19 vaccine. It is best to discuss this with your doctor.

Have patients with cutaneous lymphoma who have tested positive for COVID-19 shown increased cutaneous lymphoma disease activity afterwards?

There have only been a couple of case reports, which is a detailed report of the symptoms, signs, diagnosis, treatment, and follow-up of an individual patient, regarding this. At this time, there isn’t enough data to answer the question.

Does the lack of reaction to the vaccine correlate with patients not building antibodies?

If you don’t mount an antibody response, it is possible that the immune system response is not optimal. However, there is a whole other component of the response that is the T-cell response, which is longer lasting, but this is hard to measure. At this time, it is not known if the antibody response correlates to the actual immune response.

Please note: These FAQs were derived from a webinar hosted on 10/12/21. Please be sure to check the CDC website for the most current and up-to-date recommendations.
CUTANEOUS LYMPHOMA FOUNDATION

Sézary Syndrome…continued from pg 1

Interferons are substances which our bodies produce naturally and may be given as a form of immunotherapy. Interferons stimulate anti-cancer immune function. However, interferons bring about a wide range of responses. While there is no clear protocol when using interferons in treatment, most patients use this option for the long run, with good general effectiveness. Interferons are given by self-injection three times a week. Early in the treatment schedule, many patients report flu-like symptom reactions, which tend to improve over time. Frequent lab monitoring of blood count and liver enzymes is required on interferon. Some patients experience depression mood and mental fog which lead to termination of treatment.

There is a class of drugs termed “targeted agents” which means that the drug identifies and impairs a specific protein rather than impacting all cells broadly, as is the case with traditional chemotherapy. In general, these drugs tend to be better tolerated than older generations of chemotherapy with less nausea, vomiting, hair loss and neutropenia/immunosuppression.

Included in this group is Romidepsin, an enzyme inhibitor, which shows effectiveness in about one third of patients, although it can take over three months for progress to be noted. Romidepsin has a long infusion time, between four and five hours, and can cause some severe side effects such as fatigue and nausea for certain patients.

Protein-Targeting Drugs
Alectinib (also known as Campath) targets the CD52 protein expressed in malignant cells. Trials show a very good overall response rate when this is given as an injection, in the office, three days a week. However, this treatment may eradicate some malignant cells as well, and patients must also take prophylactic antibiotics and antiviral medication.

Another choice, this one targeting the CD50 protein, is Brentuximab, which is usually given as an infusion every three weeks. While the response rate of 60% is good, it has some possible severe side effects such as neuropathy which must be closely monitored.

Mogamulizumab, given by infusion weekly for 4 weeks, then every other week thereafter, targets the CCR4 protein molecule. The response rate is around 28%, but patients must be careful to complete a wash-out period from this medication, if they plan to schedule a stem cell treatment in the near future.

Other Treatment Options
Outside of these protein-targeting drugs, other treatment options include Total Skin Electron Beam radiation, which attempts to uniformly deliver electrons (radiation) to the entire surface of the skin. As part of a combination therapy, long-term remission has been recorded using low-dose Electron Beam Therapy along with immunotherapy.

A promising treatment option is Immunotherapy, which is designed to enhance the native anti-cancer response. Using Extracorporeal Photopheresis (ECP), blood is extracted from the patient, then lymphocytes are separated out, irradiated with ultraviolet type A light (UVA) which exoses the genetic material of the cancer cells, allowing the body to better identify the cancer cell target. The blood is then re-infused into the patient to help the patient’s immune system recognize and attack the cancer cells. ECP is given in two consecutive treatments over four or five hours every two to four weeks. Responsiveness to this treatment option varies, with highest reports around 60%. Four to five hours of continuous high flow large bore IV access is required and for some patients a port must be installed for this reason.

Immune Checkpoint Inhibitors are molecules that boost anti-cancer immune function by preventing cancer cells from evading routine immune surveillance by healthy T cells. Pembrolizumab is a PD-1 inhibitor in this category. A study completed in 2016 showed a 38% response rate in Sézary, however, some patients reported flares during the treatment. This is explained by the fact that these drugs turn on T cells in efforts to fight disease, but in CTCL when the T cells are abnormal, the drug may also stimulate the malignant T cells leading to disease worsening. As a class, these drugs augment immune activity and the main side effects are autoimmune inflammation of the thyroid, lungs, gut and rarely the heart and nervous system.

Currently, the only treatment aimed at cure rather than remission is Stem Cell Transplant (SCT) therapy. Candidates for stem cell transplant should have excellent disease control prior to undergoing the transplant. Preparation for SCT involves using drugs and radiation to eliminate the patient’s current immune system prior to engrafting a new donor immune system. The hope is that the new immune system is better able to fight Sézary. Jennifer DeSimone, MD, FAAD

Inova Schar Cancer Institute

The Sézary Syndrome Part I and 2 articles were based on Dr. DeSimone’s presentation at the 2021 Virtual Patient Conference. You can watch a recording of the presentation at: https://bit.ly/3R0r5S

To see the referenced NCCN guideline for Category A Medications, please visit: https://bit.ly/3RrK38

The Cutaneous Lymphoma Foundation was pleased to participate in the American Academy of Dermatology Association’s (AADA) Virtual Legislative Conference and Day on the Hill. As a member of the Coalition of Skin Diseases, the Foundation was invited to participate in this annual event, providing an invaluable opportunity to add the patient voice. We joined over 200 dermatologists and 40 patient advocates from 30 states to speak to members of Congress – making this one of the most well-attended AADA legislative events yet.

The AADA’s legislative “asks” were especially pertinent to the cutaneous lymphoma community:

• Ensure Medicare Stability for Patients & Physicians - members of Congress were asked to take action to prevent Medicare physician payment cuts that impact patients’ access to care and will help ensure financial stability for physician practices that are struggling from the effects of the pandemic. The relevance to patients is the potential 10% cut to Medicare payments could cause dermatologists to lay-off staff (causing long delays in getting appointments), not invest in equipment (for example phototherapy units), or limit the number of Medicare patients they will see.

• Preserve Patients Access to Treatments - the focus of this “ask” is the Safe Step Act (H.R. 2163/S. 464). Step therapy protocols or “fail first” strategies currently used by health plans prevent physicians from prescribing treatments that will provide the best treatment results in the most effective manner. Step therapy protocols require patients to try one or more prescription drugs before coverage is provided for a treatment selected by the patient’s physician. The Safe Step Act establishes an exemption process to the protocols used by health plans preventing physicians from prescribing treatments that will provide the best treatment results in the most effective manner. Step therapy protocols require patients to try one or more prescription drugs before coverage is provided for a treatment selected by the patient’s physician. The Safe Step Act establishes an exemption process to the protocols used by health plans, preserving the physician’s right to make treatment decisions in the best interest of the patient. (Summaries from AADA one-pagers prepared for members of Congress)

A highlight of each conference is recognizing the cutaneous lymphoma clinicians participating in the event. It is gratifying to know that our clinicians use their own time to advocate on behalf of the patients they serve.

If you would like to know more about how you can participate in advocacy, we recommend watching Your Voice Matters: How (and Why) to Take Action on Public Policy - the patient advocacy presentation from our recent International Patient Conference. You can find the video on our YouTube channel, CutaneousLymphomaFnd, or on our Advocacy page on the website (www.clfoundation.org/Advocacy).

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UPCOMING EVENTS & OPPORTUNITIES

Join Community Connections

Make sure to check out the Cutaneous Lymphoma Community Connections, a place where you can interact with others facing the same or similar experiences as you. In order to provide privacy and encourage open communication with each other, Community Connections is open exclusively to patients and their loved ones.

To learn more, visit www.cfjournal.org/upcoming-events or scan the QR code.
The Cutaneous Lymphoma Foundation is Your Cutaneous Lymphoma Community Center

YOUR place to belong...

• a library of educational information
• a resource center for finding specialists, clinical trials, financial aid and more
• an activity center with programs and events focused on education and connection
• a common area providing a safe space to share your experiences with peers
• a town hall to bring voices together to make change
• a research lab with a visitor gallery -- a place to invest in finding a cure, including a birds eye view into how the work is getting done

Ensure the doors stay open and the lights stay on, for you, and the next person affected by cutaneous lymphomas.

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